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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/073,596	05/06/1998	RALPH M. STEINMAN	20164000US	9977
43852	7590	12/13/2006		
MERIX BIOSCIENCE, INC. 4233 TECHNOLOGY DRIVE DURHAM, NC 27704				
			EXAMINER EWOLDT, GERALD R	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/073,596

Applicant(s)

STEINMAN ET AL.

Examiner

G. R. Ewoldt, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 89,91,92,94,95,99,101,103-121 and 123-141 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 89,91,92,94,95,99,101,103-121 and 123-141 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendments and remarks, filed 9/26/06, are acknowledges.
2. Claims 89, 91, 92, 94, 95, 99, 101, 103-121, and 123-141 are pending.
3. In view of Applicant's amendments and remarks the previous rejection of Claim 110 under the first paragraph of 35 U.S.C. 112 for the introduction of new matter has been withdrawn. Additionally, the nonstatutory double patenting rejection has been withdrawn in view of the cancellation of Claims 45 and 46 in copending Application No. 10/287,813. Also, the previous rejection of Claim 122 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of the cancellation of Claims 122.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 89, 91, 92, 94, 95, 99, 101, 103-121, and 123-141 stand/are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) An *in vitro* composition comprising antigen-activated dendritic cells presenting fragmented antigen and derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors by a method comprising:

providing a tissue source comprising dendritic cell precursors;
optionally treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors;
culturing the tissue source on a substrate in a culture medium comprising

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GM-CSF to obtain cell clusters;

~~subculturing the cell clusters to produce~~ cell aggregates comprising proliferating dendritic cell precursors; and

subculturing the cell aggregates at least one time to enrich the proportion of dendritic cell precursors;

wherein the dendritic cell precursors are cultured *in vitro* in the presence of an antigen for time sufficient to allow the antigen to be fragmented and presented (Claim 101).

B) An *in vitro* composition comprising antigen-activated dendritic cells presenting fragmented antigen derived from an *in vitro* culture of population of enriched and expanded proliferating dendritic cell precursors which were contacted *in vitro* with an antigen in the presence of GM-CSF for a sufficient time for antigen fragmentation and presentation to occur (Claim 120).

It is noted that no support for the limitations of these claims as they are now recited has been submitted. Limitations have been added amendment by amendment such that the claimed invention has evolved into one that is not supported by the specification. In particular, note that the method of Claim 101 is in general disclosed by the specification as a method of deriving mature DCs, not the antigen-activated DCs of the claims. Also note that not all the steps of the claimed method are precisely those set forth in the specification, for example, the "optional" step of treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors does not appear to be optional in the specification.

Note that in the amendment of 9/26/06 Claim 101 has been amended as reflected above.

Applicant's arguments, filed 9/26/06, have been fully considered but are not found persuasive. Applicant asserts that mature DCs and antigen-activated DCs are not unrelated and that the DCs share many properties. Applicant argues that a verbatim description is not required.

In response, note that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Regarding a verbatim description, while a verbatim description of a claimed invention may not be required, the claimed invention must be described in some manner in the specification, further, an invention that might be obvious in light of the specification would not likely be adequately described.

Applicant cites pages 9-10 in support of the claimed cells.

The cite at pages 9-10 does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

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Applicant cites page 12 in support of the claimed cells.

The cite at page 12 discloses DC precursors and not the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites pages 35-36 in support of the claimed cells.

The cite at pages 35-36 does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites page 37 in support of the claimed cells.

The cite at page 37 discloses phagocytic DC precursors and not the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites pages 5-6 in support of the claimed cells.

The cite at pages 5-6 is in the Background section and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites Example 3 in support of the claimed cells.

Example 3 discloses experiments performed with mouse DC precursors and does not disclose the generic antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites page 19-20 in support of the claimed cells.

The cite at pages 19-20 discloses DC precursors and mature DCs and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites pages 20-21 in support of the claimed cells.

The cite at pages 20-21 discloses DC precursors and sources of said precursors, and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

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Applicant cites page 24 in support of the claimed cells.

The cite at page 24 discloses "a primary culture" and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites page 25 in support of the claimed cells.

The cite at page 25 discloses precursor DCs and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites pages 27 and 28 in support of the claimed cells.

The cites at pages 27 and 28 again disclose "a primary culture" and not the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites pages 27-30 in support of the claimed cells.

The cite at pages 27-30 discloses "a primary culture", "the culture of precursor cells", a method of "producing DC [sic] from bone marrow", and a "blood derived population of DCs"; it does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

Applicant cites page 39 in support of the claimed cells.

The cite at page 39 discloses DCs and does not disclose the antigen-activated DCs of the claims nor the method of producing them set forth in the claims.

As set forth previously, while bits and pieces of the method of producing the antigen-activated DCs of the instant claims are disclosed, the method as a whole is not.

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6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 89, 91, 92, 94, 95, 99, 101, 103-121, and 123-141 stand/are rejected under 35 U.S.C. 102(a) as being anticipated by Pancholi et al. (1992).

As set forth previously, Pancholi et al. teaches a pharmaceutical composition comprising human DCs pulsed with tuberculosis antigens (see particularly page 218, last paragraph).

The reference clearly anticipates the claimed invention.

Regarding product-by-process claims, MPEP 2113 states:

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), and

"The Patent Office bears a lesser burden of proof in making out a case of *prima facie* obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983).

It is the Examiner's position that antigen-activated DCs of the instant claims are the DCs of the prior art.

Applicant's arguments, filed 9/26/06, have been fully considered but are not found persuasive. Applicant argues that Pancholi et al. is not available as art.

Applicant is advised that because the claimed cells are not supported by the instant specification they are not supported by the priority documents, thus the priority date of the instant application is its filing date, 05/06/1998.

8. The following are new grounds for rejection necessitated by Applicant's amendment.

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9. Claims 123-141 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

An *in vitro* composition comprising at least 1×10^6 antigen-activated dendritic cells presenting fragmented antigen and derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors by a method comprising:

providing a tissue source from a single donor comprising dendritic cell precursors;

optionally treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors;

culturing the tissue source on a substrate in a culture medium comprising GM-CSF to obtain cell aggregates comprising proliferating dendritic cell precursors; and

subculturing the cell aggregates at least one time to enrich the proportion of dendritic cell precursors;

wherein the dendritic cell precursors are derived from said single donor and wherein the dendritic cell precursors are cultured *in vitro* in the presence of an antigen for a time sufficient to allow the antigen to be fragmented and presented (Claim 123).

Applicant cites Examples 1 and 6 in support.

Example 1 discloses experiments performed employing mouse DCs and not the generic DCs from any source of the claim. Additionally, the Example discloses other limitations, e.g., specific dosages of rGM-CSF and specific concentrations of cells/well in culture, etc. that are not recited in the claim. Example 6 discloses experiments performed employing human DCs and not the generic DCs from any source of the claim. And again, the Example discloses other limitations, e.g., treatment with G-CSF, that are not recited in the claim.

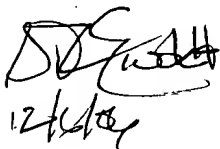
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10. No claim is allowed.

11. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600